Express Mail Label No.: EL844533552US
Date of Deposit: December 14, 2001
Attorney Docket N .: C1037/7025 (HCL/MAT)

INHIBITION OF ANGIOGENESIS BY NUCLEIC ACIDS

Related Applications

This application claims priority under 35 U.S.C. §119(e) from Provisional U.S. Patent Application Serial No. 60/255,534 filed on December 14, 2000, entitled INHIBITION OF ANGIOGENESIS BY NUCLEIC ACIDS. The entire contents of the provisional application are hereby expressly incorporated by reference.

Background of the Invention

Blood vessels are the means by which oxygen and nutrients are supplied to living tissues and waste products are removed from living tissue. Angiogenesis refers to the process by which new blood vessels are formed. See, for example, the review by Folkman and Shing, *J. Biol. Chem.* 267(16):10931-10934, 1992. Thus, where appropriate, angiogenesis is a critical biological process. It is essential in reproduction, development and wound repair. However, inappropriate angiogenesis can have severe negative consequences. For example, it is only after many solid tumors are vascularized as a result of angiogenesis that the tumors have a sufficient supply of oxygen and nutrients that permit it to grow rapidly and metastasize. Because maintaining the rate of angiogenesis in its proper equilibrium is so critical to a range of functions, it must be carefully regulated in order to maintain health. The angiogenesis process is believed to begin with the degradation of the basement membrane by proteases secreted from endothelial cells (EC) activated by mitogens such as vascular endothelial growth factor (VEGF) and basic fibroblast growth factor (bFGF). The cells migrate and proliferate, leading to the formation of solid endothelial cell sprouts into the stromal space, then, vascular loops are formed and capillary tubes develop with formation of tight junctions and deposition of new basement membrane.

In adults, the proliferation rate of endothelial cells is typically low compared to other cell types in the body. The turnover time of these cells can exceed one thousand days. Physiological exceptions in which angiogenesis results in rapid proliferation typically occurs under tight regulation, such as found in the female reproduction system and during wound healing.